IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appl. No.	:	09/555,102	Confirmation No.: 9263
Appellant	:	Nicholas Thomas	
Filed	:	July 17, 2000	
TC/A.U.	:	1641	
Examiner	:	Gailene Gabel	
Docket No.	:	PA9720	
Customer No.	:	22840	

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P.O. Box 1450
Alexandria, Virginia 22313-1450

November 8, 2004

APPEAL BRIEF

Sir:

Appellant submits this Appeal Brief, in triplicate, appealing from the November 12, 2003, rejection of the Examiner, rejecting all pending claims in the captioned application. A Notice of Appeal was filed on **April 12, 2004**, which contained authorization to charge the fee for the Notice of Appeal to Appellant's Deposit Account. Enclosed herewith is a "Transmittal of Appeal Brief (Large Entity)" containing authorization to charge the fee for filing the Appeal Brief to Appellant's Deposit Account.

In connection with the instant appeal, Appellant submits, concurrently herewith, a "Request for Oral Hearing Before the Board of Patent Appeals and Interferences" containing authorization to charge the fee for the "Request for Oral Hearing" to Appellant's Deposit Account.

REAL PARTY IN INTEREST

Amersham Biosciences (SV) Corp, owner of the captioned application, is the real party in interest to this appeal.

RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences related to the instant appeal.

STATUS OF CLAIMS

Claims 1, 3, 5-9 and 12-18 are pending in the captioned application. These claims are reproduced in Appendix A, attached hereto.

STATUS OF AMENDMENTS

The Advisory Action mailed October 25, 2004, indicates that Appellant's amendment filed **April 12, 2004** (*incorrectly listed as June 22, 2004, in the Advisory Action*), has been entered. The Examiner's intention to enter the amendment was discussed via telephone interview with the undersigned representative of Appellant on October 5, 2004 and October 25, 2004.

SUMMARY OF INVENTION

The instant invention teaches the use of encoded particles to permit parallel processing of many samples in a single analysis by flow cytometry. Encoded particles (distinguishable bead populations) are added to multiple assay vessels, wherein each vessel receives a different distinguishable bead population. However, all of the distinguishable bead populations are coated with an identical reactant (reagent) and all assay vessels are provided with identical reagents for performing an assay so that each vessel ultimately contains identical reagents to perform the same assay on all samples. Addition of the single compound to be tested (the single analyte in each sample) to each assay vessel causes the association of a detectable signal moiety with each distinguishable bead population in each assay vessel. Consequently, following pooling of samples and parallel analysis, the assay signal moiety associated with each bead population can be determined and the assay signals assigned to each identifiable assay sample vessels and its analyte. This method is an advance over prior art methods in that it permits parallel processing of multiple samples through detection instrumentation that previously could be used only in a serial fashion. The distinctions between the invention and cited prior art are further illustrated in the appended figure, labeled "ATTACHMENT #1" (*first presented with Appellant's response filed March 26, 2002*) .

Independent claim 1 and claims 3 and 5-9 depending thereon, are directed to the binding type of assay discussed by Appellant at page 7-8 of the specification. Independent claim 12 and claims 13-18 depending thereon, are directed to the chemical or enzymatic type assay discussed at pages 8-9 of the specification.

ISSUES

1. Whether claims 1, 3, 5-7, 9 and 12-16 and 18 are properly rejected under 35 U.S.C. 103 (a) as being unpatentable over Chandler et al., U.S. Patent No. 5,981,180, in view of Yamashita et al., U.S. Patent No. 6,210,900.

2. Whether claims 8 and 17 are properly rejected under 35 U.S.C. 103 (a) as being unpatentable over Chandler et al., U.S. Patent No. 5,981,180, in view of Yamashita et al., U.S. Patent No. 6,210,900, and further in view of Mandecki, U.S. Patent No. 5,641,634.

GROUPING OF CLAIMS

For purposes of analyzing the rejections under 35 U.S.C. § 103(a) all the rejected claims in the 35 U.S.C. § 103(a) rejections appealed herein stand or fall together.

ARGUMENTS

1. Claims 1, 3, 5-7, 9 and 12-16 and 18 are not properly rejected under 35 U.S.C. 103 (a) as being unpatentable over Chandler et al., U.S. Patent No. 5,981,180 (hereinafter "Chandler") in view of Yamashita et al., U.S. Patent No. 6,210,900 (hereinafter "Yamashita").

Claims 1, 3, 5-7, 9, 12-16 and 18 are rejected under 35 U.S.C. § 103(a) as being

unpatentable over Chandler in view of Yamashita. Specifically, in presenting the *prima facie* case of obviousness, the Examiner sets forth elements of the instant invention as claimed, conceding that Chandler fails to disclose the elements. The Examiner continues by presenting the disclosure of Yamashita, which in Appellant's view, fails to supply teaching or motivation to combine the references and arrive at the claimed invention. The Examiner, however, then concludes that it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the reaction samples of Chandler into a mixture and apply the analysis methods of Yamashita.

In response to the above rejection, Appellant respectfully submits that the Examiner has not established a *prima facie* case of obviousness over Chandler in view of Yamashita. In order to establish a prima facie case of obviousness the Examiner must show some suggestion or motivation to combine the Chandler and Yamashita references to arrive at Appellant's invention, including all of the inventions elements as claimed. The thrust of the Examiner's rejection is that that it would have been *prima facie* obvious to one of ordinary skill in the art to combine the samples in the method of Chandler with the analysis method taught by Yamashita. Appellant submits that the Examiner has not discharged the burden of establishing a *prima facie* case of obviousness. Appellant respectfully submits that their position is supported by the arguments below.

In response to the above rejection Appellant submits that Chandler in combination with the Yamashita reference does not teach Appellant's inventive method as claimed. Chandler lacks many of the features of Appellant's invention, as set forth by the

Examiner at the top of page 6 of the Office Action dated November 12, 2003. Yamashita does not teach the use of a method with pre-existing compounds that are not coupled to beads. Additionally, neither Chandler or Yamashita teaches the addition of multiple samples containing a single compound to be tested, as instantly claimed. These limitations are present in all of Appellant's claims, either directly or by virtue of their dependence from claim 1 or 12. This difference between Appellant's invention as claimed and the prior art must not be ignored.

The Examiner's "**Response to Arguments**" section of the Office Action dated November 12, 2003, pages 8-10, paragraphs "A" and "B", attempts to clarify why Appellant's previous arguments were not persuasive. The Examiner's main concern appears to be that the recitation "said samples each containing a single compound to be tested" in claims 1 and 12, has not been given patentable weight because, it occurs in the preamble.

In response to the Examiner's concern, Appellant points out that by entry of the amendment dated April 8, 2004, claims 1 and 12 have been amended to insert the phrase - - having a single compound to be tested, - - into step "c)" of claims 1 and 12. Therefore, claims 1 and 12 now read, in pertinent part, "dispensing one of said N samples having a single compound to be tested, into a separate, corresponding one of said N different reaction vessels,".

Appellant respectfully submits that the amendments to claims 1 and 12 discussed above, make clear that the "single compound to be tested" in each sample is an element now contained in the body of the claims. The limitation "single compound to be tested" now in step "c)" of claims 1 and 12, is present in all of Appellant's claims, either directly or by virtue of their dependence from claim 1 or 12. Appellant further points out that the application of the compound to be tested is very clearly described in the specification. For example, page 7, line 26 to page 8, line 11 describes equilibrium binding assays in which the reactant may be an immunochemical reagent or a receptor. The compounds to be screened are for example, tested for their effect on the binding, (either antagonistic or agonistic) to the second member of the binding pair. In such instances, it is therefore clear that the test compound competes with the labeled ligand for binding to its binding partner.

For purposes of completeness, Appellant now responds to the Examiner's points in the Advisory Action dated October 25, 2004, and only recently received by Appellant. Appellant respectfully submits that due to the deadline for filing this brief, there was not sufficient time to again, contact the Examiner and further discuss the Examiner's reasoning in the "**Response to Arguments**" section of the Advisory Action dated October 25, 2004, pages 3-5, numbered paragraph "6.", subparagraphs "A" and "B". However, Appellant has responded below to the Examiner's points as currently understood and invites further clarification.

Regarding subparagraph "**A)**" of the Response to Arguments section of the Advisory Action dated October 25, 2004, the Examiner states that the Chandler and Yamashita references appear to read on the claimed invention because, the claimed "N samples" are not recited as N "different" samples. While Appellant greatly appreciates the Examiner's analysis Appellant is uncertain about the meaning of the term "different" as used by the Examiner. Appellant respectfully submits that it is clear from the specification that the "N samples" are different in so far as they are dispensed "into a separate, corresponding one of said N different reaction vessels", resulting in a number ("N" is greater than or equal to 2) of separate samples (see claim 1). Thus, it is apparent that the samples are separate, individual (i.e., different) samples. However, if by the term "different" the Examiner seeks to identify whether "the single compound to be tested" in each sample is the same or different for each other separate sample then, Appellant submits that the method as disclosed and claimed encompasses both possibilities.

Appellant directs attention to the specification at page 5, lines 16-26, wherein it can be seen in the examples given that the individual samples may contain the same single compound to be tested, or may contain a different single compound in each different sample, or a different single compound per sample may be tested in replicates so that multiple samples contain the same compound, while other multiple samples contain a different compound, all within the same assay. Therefore, it can be seen that in the instant invention, the unique detectable label of each carrier bead population corresponds to a single reaction vessel or sample.

From the above discussion it can be seen that Appellant's method is clearly distinct from method of Yamashita wherein one bead identity can only correspond to one compound. This is true because, in Yamashita, each compound to be tested is synthesized on an identifiable bead. Thus, in Yamashita, compound identity/activity are uniquely associated with a single bead population, unlike the claimed method wherein bead identity corresponds to the reaction vessel or sample. Appellant is unclear as to how including a recitation of the N samples as "different" would place the claimed invention even further outside the scope of the prior art, however, Appellant invites further comment.

Regarding subparagraph "**B)**" of the Response to Arguments section of the Advisory Action dated October 25, 2004, the Examiner states that "it would have been obvious . . . to have combined the *reaction samples* in the method of Chandler into separated reaction vessels for *individual assay* and subsequently into a single mixture for flow cytometric analysis as in the method taught by Yamashita because, Yamashita specifically taught high throughput advantage in combining various *reacted samples* into a single mixture for flow cytometric analysis which allows for sorting, identification, and analysis based on *their characteristic parameters acquired after exposure with corresponding individual compounds* (emphasis added)."

In response to the above reasoning, Appellant respectfully maintains that the "reaction samples" of Chandler are <u>not</u> the reaction samples of the claimed method as Chandler teaches a <u>single sample containing multiple analytes</u>, whereas Appellant's

claims recite multiply ($N \geq 2$) "samples having a single compound to be tested." Furthermore, Appellant's claimed method is not the method of Yamashita. The claimed method seeks to identify different samples (not necessarily different compounds) that undergo reactions in the same assay. The samples in the claimed method do not acquire their identifiable characteristics only after exposure with corresponding individual compounds, as reasoned above. The samples of the claimed method are identifiable through the addition of the identifiable carrier beads as added to each corresponding different reaction vessel. Only in Yamashita, is the identifiable bead uniquely linked or tied solely to the compound. Therefore, the method of Yamashita would not readily lend itself to the types of applications exemplified in Appellants specification page 5, lines 16-26 as discussed above wherein the same compound might be analyzed in replicates.

Appellant maintains the elements of claimed invention are absent from the cited references and thus the combination of the references does not result in the claimed invention including all of the steps or elements as claimed. Moreover, no proper motivation to combine the references has been shown.

In view of the amendments and comments above and the deficiencies of the cited references, Appellant respectfully submits that the presently claimed invention is patentably nonobvious over the prior art. Therefore, Appellant respectfully submits that the above rejection cannot be sustained and should be reversed.

2. Claims 8 and 17 are not properly rejected under 35 U.S.C. 103 (a) as being unpatentable over Chandler et al., U.S. Patent No. 5,981,180, in view of Yamashita et al., U.S. Patent No. 6,210,900, and further in view of Mandecki, U.S. Patent No. 5,641,634.

Claims 8 and 17 are rejected under 35, U.S.C. § 103(a) as being unpatentable over Chandler et al., in view of Yamashita et al., and further in view of Mandecki, US 5,641,634 (hereinafter "Mandecki"). Specifically, the Examiner concedes that Chandler and Yamashita fail to disclose bead populations that are electronically labeled. The Examiner continues by presenting Mandecki, as teaching electronically encoded carrier beads. The Examiner then asserts that it would have been obvious to one of ordinary skill in the art at the time of the instant invention to electronically encode populations of beads as disclosed by Mandecki, in the method of Chandler as modified by Yamashita because, Mandecki discloses its applicability in muliplex assays. Concluding, the Examiner states that one of ordinary skill in the art would have been motivated to incorporate the teachings of Mandecki into the method of Chandler as modified by Yamashita and because, Mandecki disclosed the advantage thereof, in further detecting and differentiating increased numbers of analytes simultaneously in assays.

As discussed above, in connection with the rejection of claims 1, 3, 5-7, 9, 12-16 and 18 under 35 U.S.C. § 103(a), the Chandler and Yamashita references do not teach Appellant's inventive method as claimed. Chandler, fails to teach many of the elements of the claimed method. Yamashita does <u>not</u> teach the use of a method with pre-existing

compounds that are not coupled to beads. Additionally, neither Chandler or Yamashita teaches the addition of multiple samples containing a single compound to be tested as instantly claimed. These limitations are present in all of Appellant's claims, either directly or by virtue of their dependence from claim 1 or 12. Again, this distinction must not be ignored.

The above deficiencies of the Chandler and Yamashita references are not remedied by Mandecki. Mandecki does not provide any teachings regarding the addition of multiple samples containing a single compound to be tested. Consequently, the Examiner has not established a *prima facie* case of obviousness, with respect to the inventive method as claimed. In view of the above deficiencies of the cited references alone or in combination, the presently claimed invention is patentably nonobvious over the prior art. Thus, it is respectfully requested that the above rejection be reversed.

Appellants respectfully submit that the amendments discussed above and accompanying remarks are sufficient to overcome the rejections of record. If the Examiner has relied on other reasoning for failing to allow the present claims, then Appellant asserts that such reasoning has not been conveyed to Appellants and therefore, is not of record in the present application. Appellant can only respond to the thrust of rejections as they appear on the record.

In view of the above deficiencies of the cited references alone or in combination, Appellants submit that the presently claimed invention is patentably non-obvious over the

prior art. Therefore, Appellants respectfully submit that the above rejection cannot be sustained and should be reversed.

CONCLUSION

For the reasons advanced above, Appellants respectfully contend that the rejected claims are patentable. Therefore, reversal of all rejections is courteously solicited.

Respectfully submitted,

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Appendix A

The Rejected Claims

Claim 1 (previously presented): A method for assaying N samples, wherein N is greater than or equal to 2, said samples each containing a single compound to be tested, said method comprising:

a) providing N populations of carrier beads wherein the carrier beads of each population comprise a detectable label for distinguishing the carrier beads of each population from the carrier beads of every other population,

and

a reactant bound thereto,

wherein said reactant comprises a first component of a specific binding pair, and

said reactant being the same for said carrier beads in all of said N populations;

b) dispensing one distinguishable population of said N populations of carrier beads into a separate, corresponding one of N different reaction vessels, so that said one of N different reaction vessels contains one of said N populations, and

performing said dispensing for each population of said N populations;

c) dispensing one of said N samples having a single compound to be tested, into a separate, corresponding one of said N different reaction vessels, so that said one of N different reaction vessels contains one of said N samples and one of said N populations, and

performing said dispensing for each sample of said N samples;

d) providing in a fluid medium, in each of said N different reaction vessels, reagents for performing a binding assay and wherein said reagents are the same for all said N different reaction vessels, one of said reagents being a second component of said binding pair and wherein said second component carries a signal moiety, under conditions such that a portion of the amount of said second component carrying said signal moiety is caused to be bound to said first component during said assay, in each one of said N different reaction vessels; and

e) combining the contents of said N different reaction vessels to form a mixture, and

f) analyzing the mixture by flow cytometry

wherein

i) measurement of said signal moiety indicates at least one of the following: presence or absence of said compound to be tested, concentration of said compound to be tested, and biological activity of said compound to be tested;

and

ii) measurement of said detectable label indicates the sample containing said compound to be tested.

Claim 2 (cancelled)

Claim 3 (previously presented): The method of claim 1, wherein N is 80 – 100,000.

Claim 4 (cancelled)

Claim 5 (previously presented): The method of claim 1, wherein N is from 80 to 4000.

Claim 6 (previously presented): The method of claim 1, wherein said reactant, bound to said carrier beads is pre-coated on said carrier beads.

Claim 7 (previously presented): The method of claim 1, wherein said detectable label comprises at least one fluorescent dye.

Claim 8 (previously presented): The method of claim 1, wherein said detectable label comprises an electronic label.

Claim 9 (previously presented): The method of claim 1, wherein said signal moiety is a fluorescent dye.

Claims 10-11 (cancelled)

Claim 12 (previously presented): A method for assaying N samples, wherein N is greater than or equal to 2, said samples each containing a single compound to be tested, said method comprising:

a) providing N populations of carrier beads wherein the carrier beads of each population comprise a detectable label for distinguishing the carrier beads of each population from the carrier beads of every other population, and a reagent bound

thereto, said reagent being the same for said carrier beads in all of said N populations;

b) dispensing one distinguishable population of said N populations of carrier beads into a separate, corresponding one of N different reaction vessels, so that said one of N different reaction vessels contains one of said N populations, and performing said dispensing for each population of said N populations;

c) dispensing one of said N samples having a single compound to be tested, into a separate, corresponding one of said N different reaction vessels so that said one of N different reaction vessels contains one of said N samples and one of said N populations, and performing said dispensing for each sample of said N samples;

d) combining in a fluid medium, in each of said N different reaction vessels additional reagents for performing an assay wherein said additional reagents are the same for all said N reaction vessels, and wherein one of said additional reagents or said reagent bound to said carrier bead carries a signal moiety, under conditions such that a portion of said signal moiety is caused to be partitioned between said carrier beads and said fluid medium during said assay, in each one of said N different reaction vessels;

e) combining the contents of said N different reaction vessels to form a mixture, and

f) analyzing the mixture by flow cytometry;

wherein

i) measurement of said signal moiety indicates at least one of the following: presence or absence of said compound to be tested, concentration of said

compound to be tested, and biological activity of said compound to be tested; and

ii) measurement of said detectable label indicates the sample containing said compound to be tested.

Claim 13 (previously presented): The method of claim 12, wherein N is 80 – 100,000.

Claim 14 (previously presented): The method of claim 12, wherein N is from 80 to 4000.

Claim 15 (previously presented): The method of claim 12, wherein said reagent, bound to said carrier beads is pre-coated on said carrier beads.

Claim 16 (previously presented): The method of claim 12, wherein said detectable label comprises at least one fluorescent dye.

Claim 17 (previously presented): The method of claim 12, wherein said detectable label comprises an electronic label.

Claim 18 (previously presented): The method of claim 12, wherein said signal moiety is a fluorescent dye.